

WE CLAIM:

1. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

2. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and

- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

3 A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

4. The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

5. The cell of Claim 1 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

6. The cell of Claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

7. The cell of Claim 1 wherein the nucleotide sequences to be trans-spliced to the target pre mRNA encode a papilloma virus polypeptide.

8. The cell of claim 1 wherein the papilloma virus is an oncogenic papilloma virus.

9. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

10. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

11. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site;

- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

12. The cell of claim 9 wherein the nucleic acid molecule further comprises a 5' donor site.

13. A method of producing a chimeric RNA molecule in a cell comprising:  
contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

14. A method of producing a chimeric RNA molecule in a cell

comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

15. A method of producing a chimeric RNA molecule in a cell

comprising:

contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

16. A method of claim 13 wherein the nucleic acid molecule further comprises a 5' donor site.

17. The method of claim 13, wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

18. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

19. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.



20. A nucleic acid molecule comprising :

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and
- e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

21. The nucleic acid molecule of claim 18 wherein the nucleic acid molecule further comprises a 5' donor site.

22. The nucleic acid molecule of claim 18 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

23. The nucleic acid molecule of claim 18 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable papilloma virus polypeptide and/or a marker protein.

24. The nucleic acid molecule of claim 18 wherein the papilloma virus is an oncogenic papilloma virus.

25. The nucleic acid molecule of claim 24 wherein the papilloma virus is papilloma virus 16.

26. The nucleic acid molecule of claim 20 wherein the papilloma virus is an oncogenic papilloma virus

27. The nucleic acid molecule of claim 20 wherein the human papilloma virus is an oncogenic virus.

28. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus protein pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

29. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to papilloma virus protein pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

30. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus protein pre-mRNA expressed within the cell;

- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

31. The vector of claim 28 wherein the nucleic acid molecule further comprises a 5' donor site.

32. The vector of claim 28 wherein said vector is a viral vector.

33. The vector of claim 32 wherein in said viral vector is an adeno-associated viral vector.

34. A composition comprising a physiologically acceptable carrier and a nucleic acid molecule according to any of claims 28-33.

35. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a viral pre-mRNA expressed within the cell;

- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

36. A method for inhibiting the expression of papilloma virus pre-mRNA in a subject having cervical carcinoma comprising administering to said subject a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell; and
- b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

37. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and

- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

38. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site; and
- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

39. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and

- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.